

REMARKS

Claims 1-3, 8-10, 18-20, and 38-49 are pending.

Acknowledgements

Applicant acknowledges and appreciates that the rejection of claims 38, 39, 45, and 49 under 35 USC §102(b), as allegedly being anticipated by Sigma Chemical Company (Sigma Chemical Company Catalog, 1989, pages 914, 918, 1171, and 1243) has been withdrawn.

Applicant acknowledges the Examiner's objection to claims 44, 45, 48, and 49 in view of recitation of "polypeptide consisting of SEQ ID NO:14" or "polypeptide comprises SEQ ID NO:15." Applicant has amended the claims to obviate this objection.

Applicant acknowledges the Examiner's new ground of rejection of claims 1-3, 8-10, 18-20, 38-44, and 46-48, under 35 U.S.C. 112 second paragraph, as being indefinite in recitation of "polymorphic" or polymorphism-comprising" or "respective polymorphic amino acid positions because while referring to polymorphic positions (Xaa positions), they don't serve to adequately identify the intended residue *at* the respective polymorphic positions. Applicants have amended the claims to obviate this rejection.

The Examiner maintained the rejection of claims 1, 2, 18-20, 42, and 43, under 35 U.S.C. 112 first paragraph, as allegedly comprising new matter in view of the recitation of "wherein the fragments comprise the respective polymorphic amino acid positions..." Applicant traverses this rejection and has further amended the claim to obviate this rejection.

The Examiner maintained the rejection of claims 1, 18, and 19, under 35 USC §102(a), as allegedly being anticipated by Doherty (*Proc. Natl. Acad. Sci., USA*, 96: 10869, 1999, September; of record) in view of recitation of "polymorphism comprising fragments." Applicant has amended the claim to obviate this rejection.

The Examiner maintained the rejection of claims 1, 18, 19, and 20, under 35 USC §102(e), as allegedly being anticipated by Doherty (U.S. 6,414,130; published Jul. 2, 2002; effective filing date Jan. 20, 1999; of record). Applicant has amended the claim to obviate this rejection.

The Examiner provisionally rejected claims 1 and 18-20 on the ground of nonstatutory obviousness-type double patenting as being upatentable over claims 1-3, 8-10, 18-20, and 27-30 of copending application 09/234,208. Applicant has amended the claim to obviate this rejection.

No new matter has been added.

Claim Objections

Applicant acknowledges the Examiner's objection to claims 44, 45, 48, and 49 in view of recitation of "polypeptide consisting of SEQ ID NO:14" or "polypeptide comprises SEQ ID NO:15." Applicant has amended these claims to recite "polypeptide consisting of the amino acid sequence of SEQ ID NO:14" and "polypeptide comprises the amino acid sequence of SEQ ID NO:15," respectively, to obviate this objection. Applicant, therefore, respectfully requests withdrawal of this objection.

Rejections under 35 USC §112

Claims 1-3, 8-10, 18-20, 38-44, and 46-48 were rejected, under 35 U.S.C. 112 second paragraph, as being indefinite in recitation of "polymorphic" or polymorphism-comprising" or "respective polymorphic amino acid positions because while referring to polymorphic positions (Xaa positions), they don't serve to adequately identify the intended residue at the respective polymorphic positions.

Applicant has amended the claims to obviate this rejection. Specifically, independent claims 1, 18, and 38 have been amended to recite "and wherein the polypeptide comprises: with respect to SEQ ID NO:14, at least one of the position 6 Pro and the position 73 Asp; with respect to SEQ ID NO:19, the position 2 Ser; with respect to SEQ ID NO:20, the position 5 Pro; with respect to SEQ ID NO:21, both the position 6 Leu and the position 73 Asp; with respect to SEQ ID NO:22, the position 16 Gln; with respect to SEQ ID NO:23, the position 18 Leu; with respect to SEQ ID NO:24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO:25, the position 36 Ile; with respect to SEQ ID NO:26, the position 54 Arg; with respect to SEQ ID NO:27, the position 64 Leu; or with respect to SEQ ID NO:28, both the position 6 Pro and the position 73 Asn." Claim 42 has

been amended to recite “and wherein the polypeptide comprises at least one of the position 6 Pro and the position 73 Asp.”

Likewise, independent claims 8, 18, and 39 have been amended to recite “the polypeptide comprises: with respect to SEQ ID NO:15, at least one of the position 346 Pro and the position 413 Asp; with respect to SEQ ID NO:29, the position 342 Ser; with respect to SEQ ID NO:30, the position 345 Pro; with respect to SEQ ID NO:31, both the position 346 Leu and the position 413 Asp; with respect to SEQ ID NO:32, the position 356 Gln; with respect to SEQ ID NO:33, the position 358 Leu; with respect to SEQ ID NO:34, the position 361 Asp, Alu or Val; with respect to SEQ ID NO:35, the position 376 Ile; with respect to SEQ ID NO:36, the position 394 Arg; with respect to SEQ ID NO:37, the position 404 Leu; or with respect to SEQ ID NO:38, both the position 346 Pro and the position 73 Asn.” Claim 46 has been amended to recite “and wherein the polypeptide comprises at least one of the position 346 Pro and the position 413 Asp.”

Support for this amendment is found in the originally filed specification and is discussed in detail in relation to the Examiner’s 112 first paragraph rejection (see below). No new matter has been added.

Applicant, therefore, respectfully requests that this indefiniteness rejection be withdrawn.

Rejections under 35 USC §112

The Examiner maintained the rejection of claims 1, 2, 18-20, 42, and 43, under 35 U.S.C. 112 first paragraph, as allegedly comprising new matter in view of the recitation of “wherein the fragments comprise the respective polymorphic amino acid positions...” The Examiner states that while the Table 1 discloses variant sequences, and identifies the corresponding variant positions, it does not support a subgenus of fragments limited to fragments comprising a variant residue.

Applicant respectfully traverses this rejection because, contrary to the Examiner’s assertion, ECDIIIa variant containing polypeptides, both comprising the ECDIIIa or sub fragments thereof is indeed encompassed within the original specification teachings.

As stated above, the independent claims have been amended to delineate the variant residues, including subfragment residues. Support for this amendment is explicitly found in Table 1 on page

33 of the originally-filed specification (see also, for example, original claim 27 reciting “ECDIIIa variant sequence”). Additionally, the specification recites that “[t]his result demonstrates that in the human population there are several variations in the intron-8 encoded domain that could lead to altered biochemical and biological properties among ECDIIIa-containing protein variants” (page 32, ll. 21-23). Additionally, the specification at page 14, ll. 6-8 recites “[f]or the production of antibodies, various host animals may be immunized by injection with *e.g.*, polyhistidine-tagged ECDIIIa variant polypeptides, **truncated ECDIII a variant polypeptides**, functional equivalents of the ECDIIIa variants or mutants of the ECDIIIa region.” Additionally, the specification teaches that “PCR, or reverse transcription can be utilized to identify nucleotide variation within the ECDIIIa domain (page 17, ll. 19-20). Additionally, as stated in Dr. Gail Clinton’s Declaration of record (see page 5, paragraph 5 of Declaration of Dr. Gail Clinton 19 April 2003, of record in this case), “[t]he discovery of these novel polymorphisms was precisely the reason that the present application was filed. The Herstatin sequence of the earlier U.S. patent application (09/234,208) was already disclosed and claimed in that application, and it was the primary purpose of the present application to claim additional polymorphisms, while not claiming the previously claimed Herstatin. In Example 11 of the present application, the 1999 Doherty et al. PNAS paper (which lists the previously claimed Herstatin) was cited in the introduction. Example 11 then goes on to describe the additional, different polymorphisms by their nucleotide and deduced amino acid sequence. These additional variations in the intron-8 encoded domain were discovered in the human population and Table 1 sets forth those variants, including originally identified variant 11. Said another way, while Table 1 of Example 11 lists the Doherty et al sequence as variant 11 along with the additional polymorphisms (variants 1-10), the purpose of the table is to set forth and summarize additional variants of the intron-8 encoded domain that had been discovered to the time of the filing of this patent application.” The specification, therefore, discloses new polymorphic variants and ECDIIIa variant fragments of about 50 to about 79 amino acids. No new matter has been added. Applicant respectfully contends that given the teachings of the specification, the Examiner’s characterization is unsupported and is inconsistent with the facts. For example, the specification teaches ECDIIIa subfragments and teaches variants with the subfragment region. It

would be an absurdity to construe the facts such that Applicant would not be entitled to claim a subfragment comprising any of the variant amino acids disclosed. Applicant is the first to describe such variants and this was precisely why the present application was filed, as declared by the Applicant.

Applicant, therefore, respectfully requests reconsideration and withdrawal of this alleged new matter rejection.

Rejections under 35 USC §102(a) and (e)

The Examiner maintained the rejection of claims 1, 18, and 19, under 35 USC §102(a), as allegedly being anticipated by Doherty (*Proc. Natl. Acad. Sci., USA*, 96: 10869, 1999, September; of record) in view of recitation of “polymorphism comprising fragments.”

The Examiner also maintained the rejection of claims 1, 18, 19, and 20, under 35 USC §102(e), as allegedly being anticipated by Doherty (U.S. 6,414,130; published July 2, 2002; effective filing date Jan. 20, 1999; of record).

As discussed in detail above, the claims have been amended to clarify the identity of the variant residues at the polymorphic positions. The amendments obviate the present rejections by distinguishing the claimed subject matter from that of Doherty.

Applicant, therefore, respectfully requests reconsideration and withdrawal of these rejections.

Non-statutory Double Patenting

The Examiner provisionally rejected claims 1 and 18-20 on the ground of nonstatutory obviousness-type double patenting as being upatentable over claims 1-3, 8-10, 18-20, and 27-30 of copending application 09/234,208.

As discussed in detail above, the claims have been amended to clarify the identity of the variant residues at the polymorphic positions. The amendments obviate the present rejection by distinguishing the claimed subject matter from that of Doherty.

Applicant, therefore, respectfully requests reconsideration and withdrawal of this rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests entry of the present Amendment and allowance of all claims as provided herein above. The Examiner is encouraged to phone Applicant's attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

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